

Abstract

Methods, assays, and components are described in which biological samples can be rapidly and sensitively analyzed for the presence of species associated with neurodegenerative disease. Techniques and components are provided for diagnosis of disease, as well as for screening of candidate drugs for treatment of neurodegenerative disease. The techniques are simple, extremely sensitive, and utilize readily-available components. Binding species, capable of binding a neurodegenerative disease aggregate-forming or aggregate-forming species, are fastened to surfaces of electrodes and surfaces of particles, or provided free in solution, to bind aggregate-forming species and/or be involved in aggregation.

10

---

<sup>1</sup> MorelKopp MC, Kaplan C, proulle V, Jallu V, Melchior C, Peyruchaud O, Arousseau MH, and Kieffer N, "A three amino acid deletion", *Blood*, **90** (2) 669-677 1997.

<sup>2</sup> Zhang ZJ, Kundu GC, Yuan CJ, Ward JM, Lee EJ, DeMayo F, Westphal H, and Mukherjee AB, "Severe fibronectin-deposit renal glomerular disease in mice lacking uteroglobin", *Science*, 1997, **276** (5317) 1408-1412.

<sup>3</sup> Li XF, Himanen JP, deLlano JJM, Padovan JC, Chait BT, and Manning JM, "Mutational analysis of sickle haemoglobin (Hb) gelation", *Biotechnology and Applied Biochemistry*, 1999, **29**, 165-184.

<sup>4</sup> Ref. Rhoades E., Agarwal J., Gafni A., "Aggregation of an amyloidogenic fragment of human islet amyloid polypeptide", *Biochimica Et Biophysica Acta- Protein Structure and Molecular Enzymology*, Vol. 1476 (2) 230-238, February, 2000.

<sup>5</sup> Chene P., Bechter E., "P53 mutants without a functional tetramerization domain are not oncogenic", 1999, *Journal of Molecular Biology*, Vol. **286** (5) 1269-1274.

<sup>6</sup> Chene P., Bechter E., "P53 mutants without a functional tetramerization domain are not oncogenic", 1999, *Journal of Molecular Biology*, Vol. **286** (5) 1269-1274.

<sup>7</sup> Ryan KM, Ernst MK, Rice NR, and Vousden KH, Role of NF-kappa B in p53-mediated programmed cell death", *Nature*, 2000: **404** (6780) 892-897.

<sup>8</sup> Stommel JM, Marchenko ND, Jimenez GS, Moll UM, Hope TJ and Wahl GM, "A leucine rich nuclear export signal in the p53 tetramerization domain: regulation of subcellular localization and p53 activity by NES masking", *EMBO Journal*, 1999, **18** (6) 1660-1672.

<sup>9</sup> Nie Y, Li HH, Bula CM, and Liu XA, Stimulation of p53 binding by c-Abl requires the p53 c terminus and tetramerization", *Molecular and Cellular Biology*, 2000, **20** (3) 741-748.

<sup>10</sup> Oshima, T. et al., "Targeted disruption of the cyclin-dependent kinase 5 gene results in abnormal corticogenesis, neuronal pathology and perinatal death", *Proc. Natl. Acad. Sci. USA* **93**, 11173-11178 (1996).

<sup>11</sup> Chae, T. et al., "Mice lacking p35, a neuronal specific activator of Cdk5, display cortical lamination defects, seizures and adult lethality", *Neuron* **18**, 29-42 (1997).

<sup>12</sup> Ming-Sum Lee, Young T. Kwon, Mingwei Li, Junmin Peng, Robert M. Friedlander and Li-Heui Tsai, "Neurotoxicity induces cleavage of p35 to p25 by calpain", 2000, *Nature* **405**, pg. 360-364.